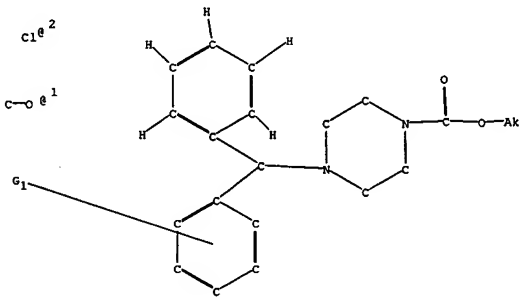
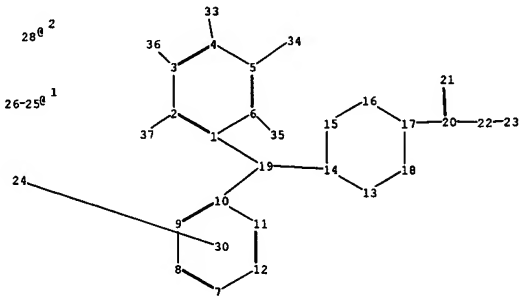
C:\Program Files\Stnexp\Queries\10076448.str

Narrow Query





chain nodes :
19 20 21 22 23 24 25 26 28 33 34 35 36 37
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
1-19 2-37 3-36 4-33 5-34 6-35 10-19 14-19 17-20 20-21 20-22 22-23 25-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14 13-18 14-15
15-16 16-17 17-18
exact/norm bonds :
13-14 13-18 14-15 14-19 15-16 16-17 17-18 17-20 20-21 20-22 22-23 25-26
exact bonds :
1-19 2-37 3-36 4-33 5-34 6-35 10-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

G1:CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,[*1],[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 28:CLASS 30:CLASS 33:CLASS
34:CLASS 35:CLASS 36:CLASS 37:CLASS

```
=>
Uploading 10076448.str

L5      STRUCTURE UPLOADED

=> s l5
SAMPLE SEARCH INITIATED 16:09:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     36 TO ITERATE

100.0% PROCESSED      36 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          360 TO     1080
PROJECTED ANSWERS:               0 TO        0

L6            0 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 16:09:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    579 TO ITERATE

100.0% PROCESSED     579 ITERATIONS                              10 ANSWERS
SEARCH TIME: 00.00.01

L7           10 SEA SSS FUL L5

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   164.87     165.08

FILE 'CAPLUS' ENTERED AT 16:10:03 ON 16 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 16 Jul 2003  VOL 139 ISS 3
FILE LAST UPDATED: 15 Jul 2003  (20030715/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l7
L8           11 L7

=> d l7 1-11 bib abs hitstr
```

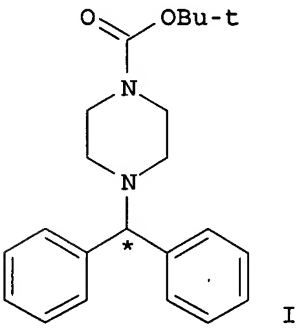
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:n

=> d l8 1-11 bib abs hitstr

L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:671907 CAPLUS
DN 137:201336
TI A process for the preparation of an optically active 4-(tert-butoxycarbonyl) piperazine compound
IN Kudo, Junko; Hirata, Norihiko; Yoshida, Tomoyasu
PA Sumitomo Chemical Company, Limited, Japan
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1236722	A1	20020904	EP 2002-251162	20020220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002249487	A2	20020906	JP 2001-46390	20010222
US 2002128275	A1	20020912	US 2002-76448	20020219
PRAI JP 2001-46390	A	20010222		

OS MARPAT 137:201336
GI

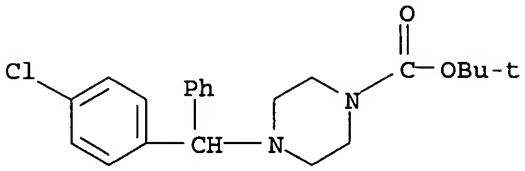


I

AB Disclosed is a process for the prepn. of I [X = Cl, alkyl, alkoxy group; * = asym. carbon atom] or a salt thereof. 1-[(4-Chlorophenyl)phenylmethyl]piperazine is converted to the Boc-deriv. (PhMe/water, Boc2O, NaOH, 35.degree.C). D-(+)-O,O'-dibenzoyltartaric acid is added to this intermediate (PhMe/MeOH, 30.degree.). The resulting mixt. is seeded and the tartrate salt of the (-)-piperazine is isolated (70.9% ee) by filtration. The ee of the salt is enriched by recrystn. with seeding. Neutralization of (-)-1-[(4-chlorophenyl)phenylmethyl]-4-(tert-butoxycarbonyl)piperazine D-(+)-O,O'-dibenzoyltartaric acid salt (98.2% ee) affords the free base of the (-)-isomer in 90% yield (98.4% ee). Deprotection is accomplished with EtOAc/HCl to afford (-)-1-[(4-chlorophenyl)phenylmethyl]piperazine dihydrochloride in quant. yield. The current process gives higher enantiomeric excess than prior art.

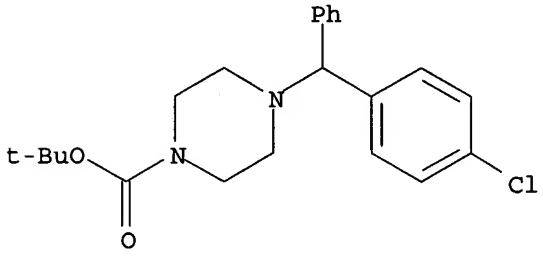
IT **454217-55-1P**, 1-[(4-Chlorophenyl)phenylmethyl]-4-(tert-butoxycarbonyl)piperazine **454217-56-2P 454217-57-3P 454217-59-5P 454217-60-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; process for prepn. of optically active 4-(tert-butoxycarbonyl) piperazine compd.)

RN 454217-55-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 454217-56-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, 1,1-dimethylethyl ester, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

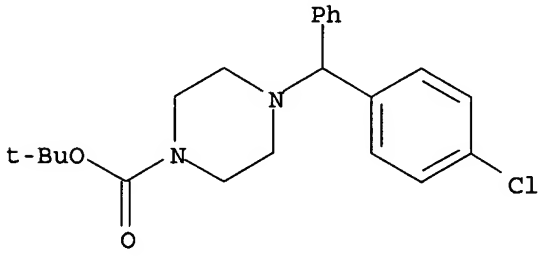


RN 454217-57-3 CAPLUS
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2S,3S)-, compd. with 1,1-dimethylethyl (-)-4-[(4-chlorophenyl)phenylmethyl]-1-piperazinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 454217-56-2
CMF C22 H27 Cl N2 O2

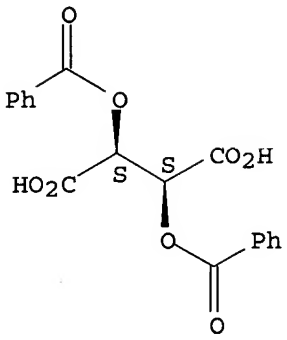
Rotation (-).



CM 2

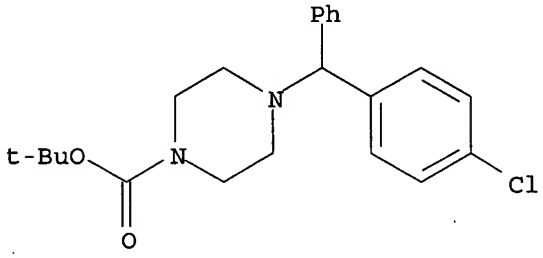
CRN 17026-42-5
CMF C18 H14 O8

Absolute stereochemistry. Rotation (+).



RN 454217-59-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, 1,1-dimethylethyl ester, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

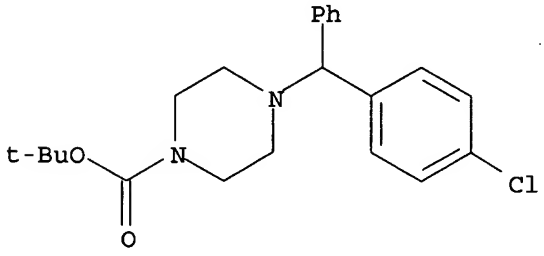


RN 454217-60-8 CAPLUS
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-, compd. with 1,1-dimethylethyl (+)-4-[(4-chlorophenyl)phenylmethyl]-1-piperazinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 454217-59-5
CMF C22 H27 Cl N2 O2

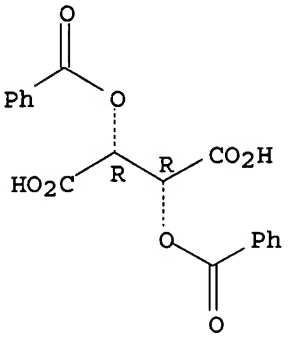
Rotation (+).



CM 2

CRN 2743-38-6
CMF C18 H14 O8

Absolute stereochemistry.



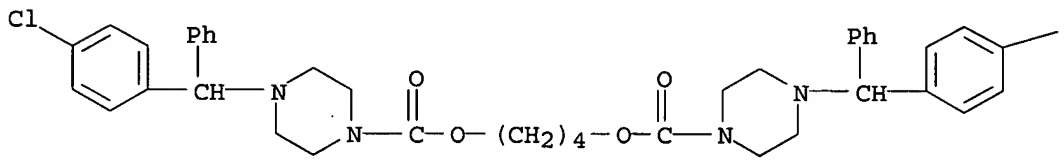
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:534072 CAPLUS
DN 137:93778
TI Preparation of multibinding H1-histamine receptor antagonists
IN Numerof, Robert P.; Ji, Yu-hua; Griffin, John H.
PA Theravance, Inc., USA
SO U.S., 77 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6420560	B1	20020716	US 1999-326627	19990607

PRAI US 1999-326627 19990607
OS MARPAT 137:93778
AB Novel multibinding compds., which are multimeric ligands, are disclosed as H1-histamine receptor antagonists. The compds. comprise 2-10 ligands, covalently connected via 1-20 linkers, with each ligand capable of binding to the H1 histamine receptor. Fourteen prophetic examples are given to illustrate the invention. Accordingly, the multibinding compds. and pharmaceutical compns. of this invention are useful in the treatment and prevention of allergic diseases such as rhinitis, urticaria, asthma, and anaphylaxis, and the like.
IT **441787-25-3P**
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of multibinding H1-histamine receptor antagonists contg. nitrogen heterocyclic ligands)
RN 441787-25-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, 1,4-butanediyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

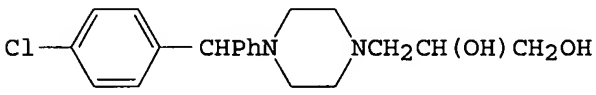
Cl

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1982:52334 CAPLUS
DN 96:52334
TI 1-(4-Chlorobenzhydryl)-4-(2,3-bishydroxypropyl)-piperazine, its use as an antitussive agent, an antihistamine, a sedative, an analgesic and an antiinflammatory agent as well as pharmaceutical preparations containing it
PA Selvi e C. S.p.A., Italy
SO Belg., 18 pp.
CODEN: BEXXAL
DT Patent
LA Dutch
FAN.CNT 1

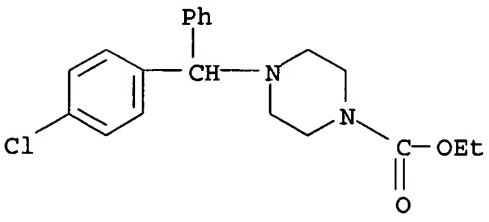
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI BE 888811	A2	19810828	BE 1981-59160	19810515
DE 3118162	A1	19820218	DE 1981-3118162	19810507
DE 3118162	C2	19840726		
FR 2482965	A1	19811127	FR 1981-9273	19810508
FR 2482965	B1	19841123		
NL 8102361	A	19811216	NL 1981-2361	19810513
GB 2076403	A	19811202	GB 1981-15827	19810522
ES 502429	A1	19820401	ES 1981-502429	19810522
JP 57031678	A2	19820220	JP 1981-78562	19810523
JP 61035189	B4	19860812		
PRAI IT 1980-22283		19800523		

GI



I

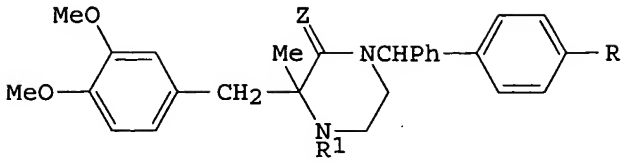
AB The title compd. was prepd. and found superior to codeine in title activity. Thus, Et 1-piperazinecarboxylate was alkylated with 4-ClC6H4CHPhBr, decarboxylated, and treated with glycidol to give I.
IT **80476-89-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and decarboxylation of)
RN 80476-89-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



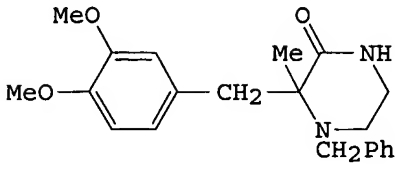
L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1976:446748 CAPLUS
DN 85:46748
TI Piperazine derivatives
IN Cyrus, Richard; Raschack, Manfred
PA Knoll A.-G., Fed. Rep. Ger.
SO Ger. Offen., 45 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2438725	A1	19760226	DE 1974-2438725	19740812
	BE 831406	A1	19760115	BE 1975-158334	19750715
	DK 7503259	A	19760213	DK 1975-3259	19750717
	DK 142871	B	19810216		
	DK 142871	C	19810921		
	FR 2281764	A1	19760312	FR 1975-22893	19750722
	FR 2281764	B1	19790810		
	ZA 7504846	A	19761027	ZA 1975-4846	19750728
	US 3996360	A	19761207	US 1975-600870	19750731
	CS 191940	P	19790731	CS 1975-5369	19750731
	SU 583754	D	19771205	SU 1975-2162172	19750804
	GB 1470362	A	19770414	GB 1975-32633	19750805
	NL 7509427	A	19760216	NL 1975-9427	19750807
	IL 47890	A1	19791031	IL 1975-47890	19750807
	DD 123340	C	19761212	DD 1975-187771	19750808
	AT 7506187	A	19770815	AT 1975-6187	19750808
	NO 7502806	A	19760213	NO 1975-2806	19750811
	NO 143221	B	19800922		
	NO 143221	C	19810102		
	SE 7508993	A	19760213	SE 1975-8993	19750811
	SE 410455	B	19791015		
	HU 172817	P	19781228	HU 1975-KO2730	19750811
	FI 7502281	A	19760213	FI 1975-2281	19750812
	FI 61698	B	19820531		
	FI 61698	C	19820910		
	JP 51043775	A2	19760414	JP 1975-98030	19750812
	AU 7583889	A1	19770217	AU 1975-83889	19750812
	ES 440208	A1	19770301	ES 1975-440208	19750812
	CA 1060446	A1	19790814	CA 1975-233316	19750812
	CH 627458	A	19820115	CH 1975-10469	19750812
	US 4031216	A	19770621	US 1976-719105	19760831
PRAI	DE 1974-2438725		19740812		
	US 1975-600870		19750731		

GI



I



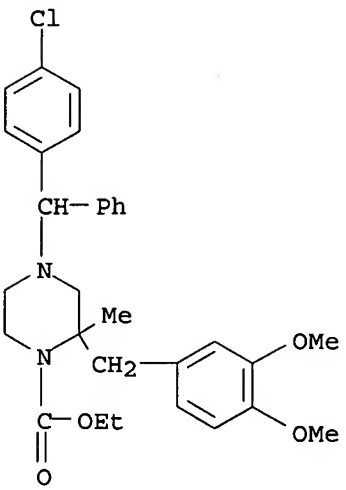
II

AB Antiarrhythmic (no data) piperazines I (R = H, Cl; R1 = C1-8 alkyl, allyl, CH2CH:CHMe, aminoalkyl, CO2Et, CH2CO2Et, Ac, hydroxyalkyl, CH2CH2O2CC6H2(OMe)3-3,4,5,Z=H2) were prepd. by alkylating I (R1 = H,Z=H2) obtained by benzylating 3,4-(MeO)2C6H3CH2CMe(CO2Me)NHCH2, treating 3,4(MeO)2C6H3CH2CMe(CO2Me)NHCH2Ph with CH2O and KCN, cyclizing 3,4-(MeO)2C6H3CH2CMe(CO2Me)N(CH2Ph)CH2CN, benzylating the piperazinone II, treating the piperazine with BrCHPh2 or ClCHPhC6H4Cl-4, debenzylating I (R1 = CH2Ph,Z = O) (III), and reducing III.

IT **59716-30-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59716-30-2 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-2-[(3,4-dimethoxyphenyl)methyl]-2-methyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



HCl

L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1960:62825 CAPLUS
DN 54:62825
OREF 54:12169a-h
TI Piperazine derivatives
IN Morren, H. G.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 549420		19570110	BE	
	DE 1062248			DE	

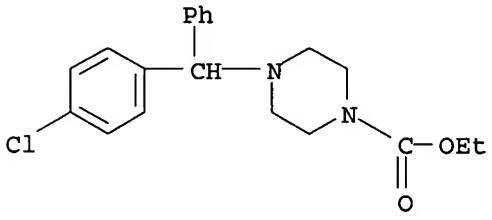
AB 1-[2-(o-Chlorobenzhydryloxy)ethyl]-4-[2-(2-hydroxyethoxy)ethyl]piperazine, b0.1 230.degree., was prepd. in 80% yield by heating at 100.degree. for 15 hrs. a stirred mixt. of 0.1 mole 1-[2-(o-chlorobenzhydryloxy)ethyl]piperazine (I), 0.11 mole Et3N, and 0.1 mole 2-(2-chloroethoxy)ethanol in 100 cc. toluene; di-HCl salt m. 150.degree.. With A = 2-(o-chlorobenzhydryloxy)ethyl group, the following derivs. were prepd.: 1-A-substituted-4-isopropylpiperazine, b0.04 184-6.degree. (di-HCl salt m. 203.degree.), in 88% yield by refluxing 1 mole 1-isopropylpiperazine, 1.1 moles Et3N, and 1 mole 2-chloroethyl o-chlorobenzhydryl ether (II) 18 hrs. in 600 cc. xylene. 1-A-Substituted-(m-methylbenzyl)piperazine, b0.1 240.degree. (di-HCl salt m. 224-6.degree.), in 50% yield, by heating under N at 160.degree. for 3 hrs., 0.1 mole 1-(m-methylbenzyl)-4-(2-hydroxyethyl)piperazine and 0.1 mole o-chlorobenzhydryl chloride. 1-A-Substituted-4-[2-(p-tert-butylbenzyloxy)ethyl]piperazine, b0.1 275.degree., in 50% yield from o-chlorobenzhydrol and 1-[2-(p-tert-butylbenzyloxy)ethyl]-4-(2-chloroethyl)piperazine at 160.degree. under N for 3 hrs. 1-A-Substituted-4-acetylpiperazine (III), b0.02 220.degree. in 94% yield from I and AcCl in presence of Et3N toluene soln. and similarly 1-A-substituted-4-(o-chlorobenzoyl)piperazine, b0.1 255.degree. (di-HCl salt m. 210-12.degree.). 1-A-Substituted-4-ethylpiperazine, b0.03 178-80.degree. (di-HCl salt m. 186-8.degree.), in 88% yield, by refluxing for 18 hrs. under N, 0.1 mole III, and 0.15 mole LiAlH4 suspended in Et2O. 1-A-Substituted-4-methylpiperazine, b0.1 185-90.degree. (di-HCl salt m. 200.degree.), in 95% yield, by treating 0.1 mole I with a soln. of 24 cc. 40% aq. HCOH in 100 cc. EtOH, and redn. in an autoclave at 60.degree. for 3 hrs. under 50 kg. H in the presence of Raney Ni. 1-A-Substituted-4-butylpiperazine b0.1 210.degree. (di-HCl salt m. 200-3.degree.). 1-A-Substituted-4-isobutylpiperazine b0.02 188-90.degree.. 1-A-Substituted-4-(2-hydroxyethyl)piperazine b0.1 230.degree.; di-HCl salt m. 150.degree.. 1-A-Substituted-4-(2,3-dihydroxypropyl)piperazine decompd. on distn.; di-HCl salt m. 147-50.degree.. 1-A-Substituted-4-cyclohexylpiperazine b0.05 235-40.degree.; di-HCl salt m. 230-3.degree.. 1-A-Substituted-4-(3-methylcyclohexyl)piperazine b0.01 230-2.degree.; di-HCl salt m. 214-15.degree.. 1 A-Substituted-4-benzylpiperazine b0.1 230-5.degree.; di-HCl salt m. 210.degree.. 1-A-Substituted-4-(o-chlorobenzyl)piperazine b0.1 240-1.degree.; di-HCl salt m. 208-9.degree.. 1-A-Substituted-4-(o-methylbenzyl)piperazine b0.005 235.degree.. 1-A-Substituted-4-(p-tert-butylbenzyl)piperazine b0.1 245-50.degree.; di-HCl salt m. 212-14.degree.. 1-[2-(o-Methylbenzhydryloxy)ethyl]-4-(o-methoxybenzyl)piperazine b0.01 234-6.degree. and the corresponding 4-isopropyl-, 4-(o-methylbenzyl)-, and 4-(m-methylbenzyl)piperazines resp. b0.002 175.degree., b0.01 218-20.degree., and b0.015 224.degree.. II, b0.1 143.degree., was obtained in 90% yield from 2-chloroethanol and chlorobenzhydrol in presence of H2SO4. Similarly prepd. was 2-chloroethyl o-methylbenzhydryl ether, b0.04 137.degree.. I, b0.007 185.degree. (di-HCl salt m. 105-7.degree.), was prepd. in 85% yield by refluxing 4 hrs. anhyd. piperazine (3.5 moles) and 1 mole II in 100 cc. xylene.

1-Cyclohexylpiperazine, b12 129-31.degree., was prepd. in 30% yield by refluxing for several hrs. cyclohexyl bromide and excess anhyd. piperazine in xylene. 1-[2-(o-Methylbenzhydryloxy)ethyl]piperazine, b0.005 168-70.degree., 1-(3-methylcyclohexyl)piperazine, b11 132-4.degree., and 1-(o-methylbenzyl)piperazine, b0.1 88.degree., were similarly prepd. 1-(2,3-Dihydroxypropyl)piperazine, b0.1 146.degree., m. 70.degree., was obtained in 40% yield by stirring below 30.degree. for several hrs., 1 mole epoxypropanol and 2 moles piperazine hexahydrate in 750 cc. H2O.

IT **80476-89-7**, 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester
(prepn. of)

RN 80476-89-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



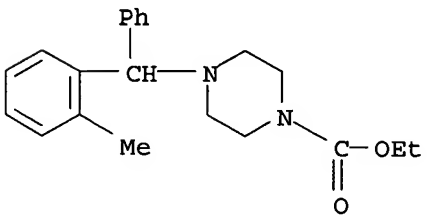
L8 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1959:122232 CAPLUS
DN 53:122232
OREF 53:21986f-i,21987a-g
TI Unsymmetrically substituted piperazines. XII. Benzhydrylpiperazines and related compounds with spasmolytic and antifibrillatory action
AU Ide, Walter S.; Lorz, Emil; Phillips, Arthur P.; Russell, Peter B.; Baltzly, Richard; Blumfeld, Robert
CS Wellcome Research Labs., Tuckahoe, NY
SO Journal of Organic Chemistry (1959), 24, 459-63
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
AB cf. C.A. 50, 4975b; 53, 11394h. In a study of compds. showing activity against artificial fibrillation, a no. of .omicron.-substituted benzhydrylpiperazines and related benzhydrylamines were prepd. The compds. were isolated, in general, by previously described techniques. The choice of mono or dihydrochlorides for the piperazines of the 1st series was largely a matter of convenience. A considerable no. of the mono-HCl salts of benzhydrylpiperazines could be crystd. from H2O and solns. have pH 5-5.5. The di-HCl salts are more readily crystd. from alc.-Et2O than the HCl salts. The following RN(CH2CH2)2NR' were prepd. (R, R', salt, and m.p. of salt given): PhCH(CH2)3Me, Me, di-HCl, 248.degree. (decompn.); PhCH(CH2)4Me, Me, di-HCl, 252.degree. (MeI deriv. m. 119.degree.); PhCHC6H11, Et (I), HCl, 266.degree.; Ph2CH, CHMe2, di-HCl, 218.degree.; MeO2CCH2CH2, Ph2CH, di-HCl, 190-1.degree.; p-H2NC6H4CO, Me, HCl, 238.degree.; p-H2NC6H4CO, PhCH2, di-HCl.2H2O, foams above 100.degree. unmelted at 250.degree.; p-H2NC6H4CO, Ph2CH, di-HCl.2H2O, foams above 100.degree. unmelted at 250.degree.; .omicron.-MeC6H4CHPh, CO2Et, HCl, 206.degree.; .omicron.-MeC6H4CHPh, H, HCl, 246.degree.; m-MeC6H4CHPh, CHMe2, di-HCl, 226.degree.; .omicron.-EtC6H4CHPh, Me, di-HCl, 223-5.degree.; .omicron.-ClC6H4CHPh, CHMe2, HCl, 272.degree.; (.omicron.-MeC6H4)2CH, Me, di-HCl, 235.degree.; (p-MeC6H4)2CH Me (II), HCl, 244-6.degree.; (.omicron.-EtC6H4)2CH, Me, di-HCl, 218.degree.; Ph3C, Me, HCl, 186-91.degree.. The following PhCHRNR2' were obtained (R, NR2', salt, m.p. of salt given): .omicron.-ClC6H4, NHMe, HCl, 214.5-15.0.degree.; .omicron.-ClC6H4, NMe2, HCl, 233-3.5.degree.; ogr;-ClC6H4, NC5H10, HCl, 240-1.degree.; .omicron.-MeC6H4, NC5H10, HCl, 265-6.degree.; .omicron.-MeC6H4, NC4H8O, HCl, 256.degree. (decompn.); .omicron.-ClC6H4, NH(CH2)2NMe2, di-HCl, 183-5.degree.; .omicron.-MeC6H4, NH(CH2)2NMe2, di-HCl, 199-200.degree.; Ph, NH(CH2)2NMe2, di-HCl, 206-7.degree.; Ph, NH(CH2)2NC4H8O, di-HCl, 243-4.degree.. The following PhCHRN(CH2)2NR'R2X were obtained (R, R', R2, X, and m.p. given): Ph, Me, C7H15 Br, 183.degree.; p-ClC6H4, Me, C7H15, BrCl, 198.degree.; p-ClC6H4, Me, C12H25, BrCl, 156.degree.; C6H11, Me, Me, iodide, 214-15.degree.; C6H11, Me, Et, iodide, 173-4.degree.; C6H11, Me, C3H7, iodide, 182.degree.; C6H11, Me, iso-Pr, iodide, 194.degree.; C6H11, Me, Bu, iodide, 108-10.degree.; C6H11, Et, Et, iodide (III), 195.degree.; C6H11, Et, iso-Pr, iodide, 216.degree.. Hexahydrobenzhydrol (19.1 g.) in 100 cc. PhMe refluxed 1 hr. with 10 cc. SOCl2, left overnight, the volatiles removed, and the residual oil distd. at 1 mm. gave 16 g. hexahydrobenzhydryl chloride (IV), b. 99.5-102.degree.. IV contained no significant amt. of unsatd. hydrocarbon. IV (8.3 g.) refluxed 96 hrs. with 9.1 g. N-ethylpiperazine, the mixt. partitioned between Et2O and H2O, the Et2O layer evapd. and shaken with N HCl, and the base liberated gave I. I (1.6 g.) in 10 cc. Me2CO left 1 day with 2 g. EtI gave 1.3 g. III. IV (10 g.) refluxed 23.5 hrs. with 20 g. N-methylpiperazine in 100 cc. MeCN, refrigerated, and sepd. gave 8.4 g. II, m. 244-6.degree. (decompn.) (abs. alc.). Pyrrolidine (10 g.) refluxed 1 hr. with 12.5 g. Ph2CHCOCl in 50 cc. Me2CO gave N-diphenylacetylpyrrolidine (V), m. 162-3.degree.

(Et2O-MeOH). V (7.9 g.) refluxed 5 hrs. with 1.5 g. LiAlH4 in 200 cc. Et2O, 5 cc. H2O added slowly, the Et2O ext. washed with dil. HCl, and the base liberated from the aq. layer gave N-(.alpha.,.alpha.-diphenylethyl)pyrrolidine, m. 174-5.degree. (Me2CO-Et2O). N-Diphenylacetyl-N'-methylpiperazine (8.8 g.) reduced as above with 2.5 g. LiAlH4 gave N-diphenylethyl-N'-methylpiperazine; di-HCl salt m. 256-7.degree. (decompn.). Diphenyl-4-pyridylcarbinol (13 g.) in 150 cc. MeOH refluxed 22 hrs. with 7 cc. MeI gave .alpha.,.alpha.-diphenylpyridine-4-methanol methiodide, m. 234-5.degree. (MeOH-Et2O). .alpha.,.alpha.-Diphenylpiperidine-4-methanol (14 g.) with 20 cc. Me acrylate in 25 cc. C6H6 kept 24 hrs. at 45-50.degree., refluxed 5 hrs., and evapd. in vacuo gave .alpha.,.alpha.-diphenyl-1-(carbomethoxyethyl)piperidine-4-methanol, m. 93-4.degree. (C6H6hexane). Methylation of the secondary base with excess MeI and alkali gave .alpha.,.alpha.-diphenyl-1-methylpiperidine-4-methanol-MeI, m. 219-20.degree. (Me2CO then alc.), .omicron.-MeC6H4MgBr (from 3.7 g. Mg and 28 g. .omicron.-MeC6H4Br) treated during 15 min. with 8 g. Me N-methylisonipecotate, left 2 hrs. at room temp., and refluxed 1 hr. gave after treatment with HCl gas 15-17 g. 1-methyl-4-(.omicron.-methylbenzoyl)piperidine (VI), m. 183-5.degree. (alc.-Et2O). Examn. of the material in the mother liquors gave 2 g. .alpha.,.alpha.-di(.omicron.-tolyl)-1-methylpiperidine-4-methanol (VII), m. 300-2.degree.. From the mother liquors of the above carbinol more material was obtained, m. 158.degree., which had the compn. of a ketone-HCl, possibly isomeric with VI or a dimorphism effect. VII was recovered after refluxing 2 hrs. with an equal vol. of AcOH or concd. HCl. With concd. H2SO4 on the steam bath VII suffered extensive decompn. Benzhydryl chloride (5 g.) and 7.2 g. N-methyl-N'-(hydroxyethyl)piperazine in a little C6H6 was warmed 3 days on the steam bath, the mixt. partitioned between Et2O and H2O, and the base in the Et2O layer converted into the HCl salt, m. 200.degree.. Treatment of an aq. soln. of the salt with alkali and excess MeI in Et2O gave N-benzhydryloxyethyl-N',N'-dimethylpiperazinium iodide, m. 182-5.degree. (alc. Et2O).

IT **112350-85-3**, 1-Piperazinecarboxylic acid, 4-(o-methyl-.alpha.-phenylbenzyl)-, ethyl ester, hydrochloride
(prepn. of)

RN 112350-85-3 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-(o-methyl-.alpha.-phenylbenzyl)-, ethyl ester, hydrochloride (6CI) (CA INDEX NAME)



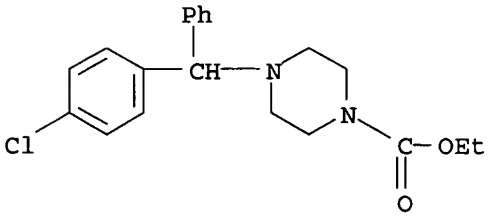
● HCl

L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1959:40048 CAPLUS
DN 53:40048
OREF 53:7215f-i,7216a-c
TI Piperazine derivatives
IN Weston, Arthur W.; Hamlin, Kenneth E., Jr.
PA Abbott Laboratories
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2861072		19581118	US	

GI For diagram(s), see printed CA Issue.
AB R2R3R4CN.CH2.CH2.NR1.CH2.CH2 (I) were prepd., some of which are useful in combating the symptoms of histamine activity while others show antispasmodic activity. p-ClC6H4CHPhCl (11.9 g.), 5.0 g. N-methylpiperazine, and 5.3 g. Na2CO3 in 75 cc. anhyd. xylene refluxed and stirred 60 hrs., the xylene layer extd. several times with dil. HCl, the exts. combined, made alk. with NaOH, extd. with Et2O, the exts. combined, dried, and treated with gaseous HCl gave I (R1 = Me, R2 = H, R3 = Ph, R4 = p-ClC6H4) (II).2HCl, m. 221.degree. (abs. EtOH-Et2O) [II.HCl, m. 223-4.degree. (abs. EtOH.)]. The following I were similarly prepd. [R1, R2, R3, R3, m.p.(or b.p.), and m.p. of di-HCl salt (or other deriv. given)]: Me, H, Ph, p-Br C6H4, b0.5 161-71.degree., 249-50.degree.; Me, H, Ph, Ph, 105-8.degree., 258-60.degree.; Me, H, Ph, p-MeOC6H4, b0.7 168-9.degree., 194-5.degree.; Me, H, p-ClC6H4, p-ClC6H4, -, 245-6.degree.; HOCH2CH2, H, Ph, Ph, -, 229.degree.; Et, H, Ph, Ph, -, 241.degree. (decompn.); Me2NCH2CH2, H, Ph, Ph, b0.7 158-62.degree., 255-7.degree. (decompn.); Me, H, Ph, p-IC6H4, b0.5 181.degree., 260-1.degree. (mono-HCl salt); H, H, Ph, Ph, 70-2.degree. (b1 183-90.degree.), 195.degree. (decompn.) (d-tartaric acid salt); Me, H, Ph, 2-pyridyl, 95-7.degree., -; Me, H, Ph, p-FC6H4, b0.6 140-1.degree., 230-1.degree. (mono-HCl salt); Me, H, Ph, p-MeC6H4, b1 159-60.degree., 228-9.degree. (mono-HCl salt); Me, H, p-ClC6H4, cyclohexyl, -, 278-9.degree. (decompn.); Et, H, Ph, p-ClC6H4, -, 227.5-8.0.degree.; Me, H, Ph, .omicron.-ClC6H4, b2 179-80.degree., 272-3.degree. (mono-HCl salt); Me, H, Ph, 2-thienyl, -, 202.degree. (decompn.); Bu, H, Ph, Ph, -, 248.degree. (decompn.); Bu, H, Ph, p-ClC6H4, -, 253.5-5.0.degree. (di-HBr salt); Me, H, Ph, m-ClC6H4, b1.5 177.degree., 249-50.degree. (mono-HCl salt); HOCH2, H, Ph, Ph, -, 189-90.degree.; Me, H, p-ClC6H4, 2-thienyl, -, 216.degree. (decompn.) (dioxalate); HO(CH2)4, H, Ph, p-ClC6H4, -, 211-12.degree. (decompn.); Me, Me, Ph, Ph, b0.7 162-5.degree., 203-5.degree. (contg. 1 H2O); H2NC(:NH), H, Ph, Ph, -, 294-5.degree. (sulfate); EtO2C, H, Ph, p-ClC6H4, -, -; EtO2C, H, Ph, Ph, 114.degree., -. Other compds. reported were: II, b0.1 150-2.degree.; II.MeI, m. 119-20.degree. (decompn.); HO(CH2)4N.CH2.CH2.N(CO2Et).CH2.CH2, b0.4 168.degree. (mono-HCl salt, m. 118-19.degree.); p-FC6H4CHPhCl, b1, 125-7.degree.; p-IC6H4CHPhCl, b0.6 148-9.degree.; .alpha.-(2-pyridyl)benzyl chloride, b0.3 126-31.degree.; .alpha.-cyclohexyl-p-chlorobenzyl chloride, b1.0 134-6.degree.; .alpha.-(2-thienyl)-p-chlorobenzyl chloride, unstable oil; p-ClC8H4ChPhN(CH2CH2Cl)2 HCl salt, m. 135-7.degree.; p-ClC6H4CHPhN(CH2CH2OH)2, b0.1 197-207.degree.; .alpha.-cyclohexyl-p-chlorophenylmethanol, b0.7 122-5.degree. m. 70-1.degree.; .alpha.-(2-thienyl)-p-chlorobenzyl alc., b0.3 157-8.degree., m. 58.5-60.0.degree.; Ph2CMeNH2, b4 140-2.degree. (di-HCl salt, m. 245-6.degree.); BuN.CH2.CH2. NH.CH2.CH2, b. 192-5.degree.; HO(CH2)4N.CH2.CH2.NH.CH2. CH2, b6 142.degree.; p-ClC6H4CHPhN.CH2.CH2.O.CH2.CH2, b0.3 162-5.degree..
IT **80476-89-7**, 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-

phenylbenzyl)-, ethyl ester
(prepn. of)
RN 80476-89-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



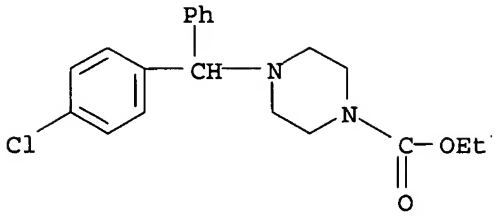
L8 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1958:88366 CAPLUS
DN 52:88366
OREF 52:15598e-i,15599a-c
TI Benzhydryl carbalkoxy piperazines
IN Weston, Arthur W.; Hamlin, Kenneth E.
PA Abbott Laboratories
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2819269		19580107	US	

AB N-Benzhydryl-N1'-carbalkoxypiperazines of the formula R2R3R4CN.CH2.CH2.NR1.CH2.CH2, where R1 is a 1-4 C atom carbalkoxy group, R2 is H or 1-4 C atom alkyl, R3 is phenyl or halophenyl and R4 is phenyl, halophenyl, pyridyl, thienyl or cyclohexyl, are prepd. by treating a benzhydryl halide with an N-carbalkoxypiperazine. N-Carbethoxypiperazine (1) (29.8 g.), 46.5 g. benzhydryl bromide, 21.2 g. Na2CO3, and 125 cc. dry xylene are refluxed 4 hrs. to yield N-benzhydryl-N'-carbethoxypiperazine (II), m. 114.degree.. II refluxed with concd. HCl or KOH yields N-benzhydrylpiperazine (III); e.g., 14 g. II and 56 g. KOH are refluxed 22 hrs. in 250 cc. 95% EtOH, the EtOH is removed in vacuo and the residue treated with H2O, extd. with Et2O and the extract dried. III distils at 183-90.degree./1 mm. and then crystallizes, m. 70-2.degree.. The d-tartrate of III, after recrystn. (abs. EtOH) melts at 195.degree. (decompn.). I, after refluxing with p-chlorobenzhydryl chloride in PhMe in presence of NaHCO3, drying and treating with dry HCl gives the white solid N-(p-chlorobenzhydryl)-N'-carbethoxypiperazine-2HCl. This can be hydrolyzed and decarboxylated, by refluxing with concd. HCl, to the N-p-chlorobenzhydrylpiperazine (IV), b. 224.degree./1 mm. Benzhydrylpiperazines with the R1 = Me or Et may be prepd. by reacting the desired piperazine with HCHO (or its polymer) or MeCHO in conjunction with HCO2H. Thus 30 g. IV, 10.3 g. 35% HCHO, and 7.6 g. 90% HCO2H are heated 3 hrs. on a steam bath and then refluxed 4.5 hrs.; 7.7 g. concd. HCl is added and excess HCHO and HCO2H distd. in vacuo. The residue is dissolved in H2O and made alk. with aq. 40% NaOH. The sepd. oil is extd. 3 times with C6H6, the extracts concd., and the residue distd. N-(p-Chlorobenzhydryl)-N'-methylpiperazine (V) distd. at 178-81.degree./1 mm.; HCl salt, m. 221-2.degree.. The N'-ethylated roduct is prepd. similarly; the di-HCl salt, m. 227-8.degree.. Zn and HCl or Raney Ni in abs. EtOH may be used instead of HCO2H to reduce the aldehyde. The N'-alkylated compds. are useful in combating symptoms of histamine activity.

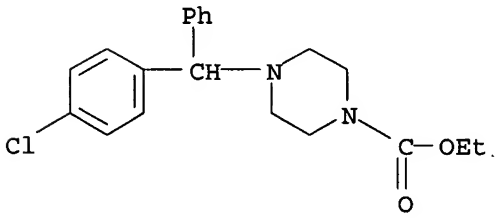
IT **111585-42-3**, 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester, dihydrochloride
(prepn. of)

RN 111585-42-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester, dihydrochloride (6CI) (CA INDEX NAME)



● 2 HCl

L8 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1958:24801 CAPLUS
DN 52:24801
OREF 52:4417e-g
TI Nonaqueous titration of 1,4-disubstituted piperazines
AU Ciaccio, L. L.; Missan, S. R.; McMullen, W. H.; Grenfell, T. C.
CS Chas. Pfizer & Co., Inc., Brooklyn, NY
SO Anal. Chem. (1957), 29, 1670-3
CODEN: ANCHAM; ISSN: 0003-2700
DT Journal
LA Unavailable
AB Potentiometric titrations of some 1,4-disubstituted derivs. with HClO4 in HOAc give 1 end point in HOAc solvent, but both end points in MeCN or MeNO2. The efficacy of 1,4-substituents in reducing strength decreases in the order EtOOC > Ph > p-chlorobenzhydryl > PhCH2, HOCH2CH2OCH2CH2, H. Thus, 4-substituted 1-carbethoxypiperazines are monobasic, 1,4-diphenylpiperazine gives 2 end points in HOAc and 1 in the weaker acid solvent MeNO2, and piperazine gives 1 end point corresponding to a dibasic base. By appropriate solvent choice differentiation according to base strength is possible.
IT **80476-89-7**, 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester
(titration of)
RN 80476-89-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1957:52175 CAPLUS
DN 51:52175
OREF 51:9717a-i,9718a-c
TI N,N'-Disubstituted-piperazines
PA Abbott Laboratories
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 752331		19560711	GB	

AB N,N'-Disubstituted-piperazines (I) were prepd. by treating Ph2CHCl or its substituted derivs. with substituted N-piperazines. Thus, refluxing and stirring a mixt. contg. 11.9 g. Ph(p-ClC6H4)CHCl, 50 g. N-methylpiperazine, and 5.3 g. Na2CO3 in 75 ml. anhyd. xylene 60 hrs., extg. the hydrocarbon layer several times with dil. HCl, making the combined washings alk. with NaOH, extg. the oil with Et2O, drying, pptg. the di-HCl salt with gaseous HCl, and recrystg. from abs. EtOH-Et2O gave N-(p-chlorobenzhydryl)-N'-methylpiperazine, m. 220-1.degree.; HCl salt, m. 223-4.degree.. Similarly were prepd. the following I (N- and N'-substituents, b.p., and, in parenthese, salt formed and its m.p., given): Ph(p-BrC6H4)CH, Me, b0.5 161-71.degree. [di-HCl salt, 249-50.degree. (from abs. EtOH)]; Ph2CH, Me, - (m. 105-8.degree.) [di-HCl salt, 258-60.degree. (from abs. EtOH)]; Ph(p-MeOC6H4)CH, Me, b0.7 168-9.degree. [di-HCl salt, 194-5.degree. (from iso-PrOH-Et2O)]; (p-ClC6H4)2CH, Me, - [di-HCl salt, 245-6.degree. (from EtOH)]; Ph2CH, HOCH2CH2, - [di-HCl salt, 229.degree. (decompn.)]; Ph2CH, Et, - [di-HCl salt, 241.degree. (decompn.)]; Ph2CH, Me2NCH2CH2, - [di-HCl salt, m. 255-7.degree. (decompn.) (from iso-PrOH-Et2O)]; Ph(p-IC6H4)CH, Me, b0.5 181.degree. (HCl salt, 260-1.degree.); .alpha.-(2-pyridyl)benzyl, Me, m. 95-7.degree.; Ph(p-FC6H4)CH, Me, b0.6 140-1.degree. (HCl salt, 230-1.degree.); Ph(p-MeC6H4)CH, Me, b1.0 159-60.degree. [HCl salt, 228-9.degree. (decompn.) (from abs. EtOH)]; C6H11(p-ClC6H4) CH, Me, - [di-HCl salt, 278-9.degree. (decompn.) (from EtOH)]; Ph(p-ClC6H4)CH, Et, - [di-HCl salt, 227.5-8.0.degree. (from EtOH-Et2O)]; Ph(o-ClC6H4)CH, Me, b2.0 179-80.degree. (HCl salt, 272-3.degree.); .alpha.-(2-thienyl)benzyl, Me, - [di-HCl salt, 202.degree. (decompn.) (from EtOH-pentane)]; Ph2CH, Bu, - [di-HCl salt, 248.degree. (decompn.) (from MeOHMe2CO)]; Ph(p-ClC6H4)CH, - [di-HBr salt, 253.5-5.0.degree. (from iso-PrOH)]; Ph(m-ClC6H4)CH, Me, b1.5 177.degree. [HCl salt, 249-50.degree. (from abs. EtOH)]; Ph2CH, HOCH2, - [HCl salt, 189-90.degree. (from EtOH-Et2O)]; .alpha.-(2-thienyl)-p-chlorobenzyl, Me, - [dioxalate, 216.degree. (decompn.)]; Ph(p-ClC6H4)CH, HO(CH2)4, - [di-HCl salt, 211-12.degree. (decompn.) (from EtOH-Et2O)]; Ph2CMe, Me, b0.7 162-5.degree. [di-HCl salt-H2O, 203-5.degree. (from abs. EtOH)]; Ph2CH, guanyl, - [H2SO4 salt, 294-5.degree. (decompn.)]; Ph(p-ClC6H4)CH, Me, - [MeI salt, 119-20.degree. (decompn.) (from abs. EtOH)]; Ph(p-ClC6H4)CH, Me, b0.1 150-2.degree. [HCl salt, 223-4.degree. (decompn.)]. The following I were also prepd. (N- and N'-substituents shown; no phys. data reported): Ph2CH, iso-Pr; Ph2CH, iso-Bu; Ph2CH, HO(CH2)3; Ph2CH, Me2N(CH2)4; Ph2CH, Me2NCH2CH2; Ph2CEt, Me; Ph2CBu, Me; (p-IC6H4)2CH, Me; (o-ClC6H4)2CH, Me; p-ClC6H4(p-BrC6H4)CH, Me; p-BrC6H4(p-MeOC6H4)CH, Me; p-ClC6H4(p-MeC6H4)CH, Me; (p-MeC6H4)2CH, Me; (p-MeOC6H4)2CH, Me; .alpha.-cyclopentylbenzyl, Me; .alpha.-(2-pyrimidyl)benzyl, Me; .alpha.-(2-furyl)benzyl, Me; Ph(p-ClC6H4)CH, EtO2C. Intermediates for the prepn. of I by alternative methods are given. Thus, refluxing 29.8 g. N-carbethoxypiperazine, 46.5 g. Ph2CHBr, and 21.2 g. Na2CO3 in 125 ml. xylene gave N-benzhydryl-N'-carbethoxypiperazine(II),m, 114-15.degree.. Refluxing 14 g. II and 56 g. KOH in 250 ml. 95% EtOH 22 hrs., concg. in vacuo, treating the residue with H2O, extg. with Et2O,

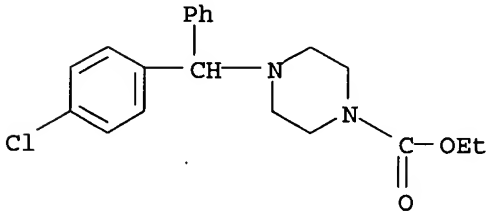
drying, and distg. gave N-benzhydrylpiperazine, b1.0 183-90.degree., which crystallizes and m. 70-2.degree.; d-tartaric acid salt, m. 195.degree. (decompn.) (from abs. EtOH). Refluxing 47.4 g. N-carbethoxypiperazine, 32.6 g. Cl(CH2)4OH, and 31.8 g. Na2CO3 in 150 ml. anhyd. EtOH 5 hrs. gave N-carbethoxy-N'-(4-hydroxybutyl)piperazine (III), b0.4 165-8.degree. (HCl salt, m. 118-19.degree.). Hydrolyzing 24 g. III in 100 ml. concd. HCl gave N-(4-hydroxybutyl)piperazine, b6.0 142.degree.. Dissolving 82 g. Ph(p-FC6H4)CHOH in 50 ml. C6H6 and 50 ml. n-hexane, mixing with excess CaCl2, treating with HCl, cooling, keeping the temp. at 12-25.degree., pouring the soln. over a fresh batch of CaCl2, repeating in 15 min., filtering, concg., and distg. the residue gave Ph(p-FC6H4)CHCl, b1.0 125-7.degree.. Similarly Ph(p-IC6H4) CHCl, b0.6 148-9.degree., was prepd.

Treating a cooled mixt. of 24 g. .alpha.-(2-pyridyl)benzhydryl alc. HCl salt in 200 ml. anhyd. C6H6 with 36 g. SOCl2, stirring 1 hr., allowing to stand at room temp. 15 hrs., heating 1 hr. at 60.degree., concg. in vacuo, removing the excess SOCl2 by repeated addn. of anhyd. C6H6, distg. in vacuo, dissolving the residue in H2O, making alk. with Na2CO3, extg. with Et2O, and distg. gave .alpha.-(2-pyridyl)benzhydryl chloride, b0.3 126-31.degree.. Refluxing 23.7 g. Ph(p-ClC6H4)CHCl, 10.5 g. (HOCH2CH2)2NH, and 10.6 g. Na2CO3 in 150 ml. dry PhMe 40 hrs., decanting the supernatant liquid, concg., and distg. the yellow oil gave Ph(p-ClC6H4)CHN(CH2CH2OH)2, b0.1 197-207.degree. (HCl salt, m. 135-7.degree.. Adding 70.3 g. p-ClC6H4CHO to a Grignard reagent prepd. from 114.1 g. cyclohexyl bromide and 14.4 g. Mg, decompg. the addn. complex with NH4Cl, extg. with Et2O, and distg. gave the carbinol, b0.7 122-5.degree., which on standing solidifies and m. 70-1.degree.; treatment with HCl gave .alpha.-cyclohexyl-p-chlorobenzyl chloride, b1.6 134-6.degree.. Similarly prepd. was the .alpha.-(2-thienyl) analog which decomp. on heating. Adding 45 g. MeCPh2CONH2 to an alk. hypobromite soln. prepd. from 33.6 g. Br and 82 g. KOH in 425 ml. cold H2O, stirring 1 hr. at 0.degree., gradually warming to room temp., then on a steam bath 30 min., extg. the yellow oil with Et2O, drying, concg., and distg. the residue gave MeCPh2NH2, b4 140-2.degree.; HCl salt, m. 245-6.degree.. Refluxing 33 g. N-carbethoxy-N'-butylpiperazine in 170 ml. concd. HCl 42 hrs., concg. in vacuo, dissolving the residue in warm H2O, making alk. with 50% KOH, extg. the oil layer with Et2O, drying, and distg. gave N-butylpiperazine, b747 192-5.degree.. The compds. are useful in combating symptoms of histamine and have antispasmodic activity.

IT **80476-89-7**, 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester
(prepn. of)

RN 80476-89-7 CAPLUS

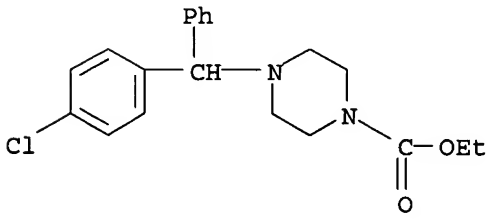
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1957:30115 CAPLUS
DN 51:30115
OREF 51:5847a-b
TI N-Diarylmethylpiperazines
PA Abbott Laboratories
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 752332		19560711	GB	

GI For diagram(s), see printed CA Issue.
AB N-Diarylmethyl-N'-carbalkoxypiperazines were hydrolyzed and decarboxylated by refluxing with concd. HCl or KOH in EtOH. Thus, p-ClC6H4PhCHN.(CH2)2.N(CO2Et).CH2.CH2, prepd. from N-carbethoxypiperazine and 4-ClC6H4PhCHCl refluxed with concd. HCl gave N-p-chlorobenzhydrylpiperazine. Similarly, N-benzhydryl-N'-carbethoxypiperazine refluxed 22 hrs. in KOH-EtOH gave benzhydrylpiperazine, b1 183-90.degree., m. 70-2.degree..
IT **80476-89-7**, 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester
(and its decarboxylation)
RN 80476-89-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)

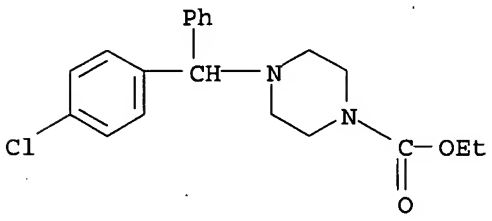


```
=> file caold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    50.73     215.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -7.16      -7.16

FILE 'CAOLD' ENTERED AT 16:11:27 ON 16 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  This file supports REG1stRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

=> s l8
L9            7 L7

=> d l9 1-7 bib hitstr
```

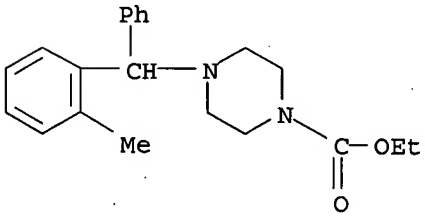
L9 ANSWER 1 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA54:12169h CAOLD
TI substituted methylpiperazines
AU Janssen, Paul A. J.
DT Patent

PATENT NO.	KIND	DATE
BE 539693		

IT **80476-89-7**
RN 80476-89-7 CAOLD
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 2 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA53:21986f CAOLD
TI unsymmetrically substituted piperazines - (XII) benzhydrylpiperazines and related compds. with spasmolytic and antifibrillatory action
AU Ide, Walter S.; Lorz, E.; Phillips, A. P.; Russell, P. B.; Baltzly, R.; Blumfeld, R.
IT **112350-85-3**
RN 112350-85-3 CAOLD
CN 1-Piperazinecarboxylic acid, 4-(o-methyl-.alpha.-phenylbenzyl)-, ethyl ester, hydrochloride (6CI) (CA INDEX NAME)

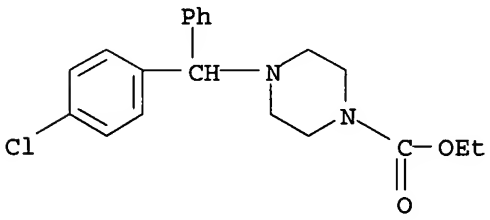


● HCl

L9 ANSWER 3 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA53:7215f CAOLD
TI piperazine derivs.
AU Weston, Arthur W.; Hamlin, K. E.
PA Abbott Laboratories
DT Patent

PATENT NO.	KIND	DATE
US 2861072		1958

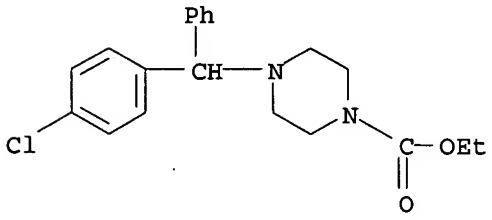
IT **80476-89-7**
RN 80476-89-7 CAOLD
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA52:15598e CAOLD
TI benzhydryl carbalkoxy piperazines
AU Weston, Arthur W.; Hamlin, K. E.
PA Abbott Laboratories
DT Patent

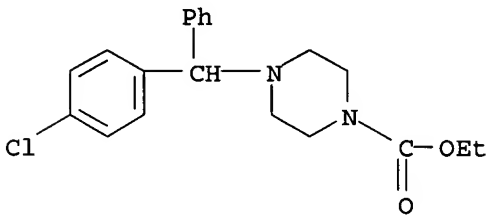
PATENT NO.	KIND	DATE
US 2819269		1958

IT **111585-42-3**
RN 111585-42-3 CAOLD
CN 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester, dihydrochloride (6CI) (CA INDEX NAME)



●2 HCl

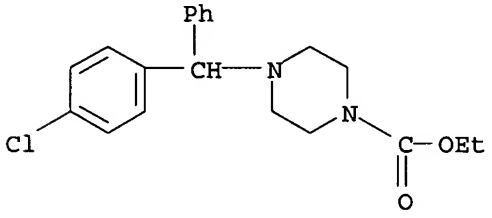
L9 ANSWER 5 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA52:4417f CAOLD
TI nonaq. titration of 1,4-disubstituted piperazines
AU Ciaccio, L. L.; Missan, S. R.; McMullen, W. H.; Grenfell, T. C.
IT **80476-89-7**
RN 80476-89-7 CAOLD
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



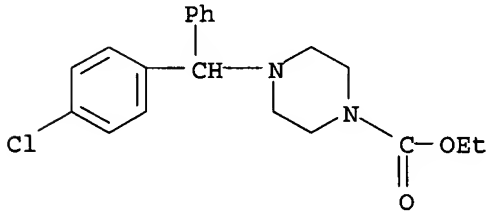
L9 ANSWER 6 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA51:9717a CAOLD
TI N,N'-disubstituted-piperazines
PA Abbott Laboratories
DT Patent

PATENT NO.	KIND	DATE
GB 752331		

IT **80476-89-7 111585-42-3**
RN 80476-89-7 CAOLD
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 111585-42-3 CAOLD
CN 1-Piperazinecarboxylic acid, 4-(p-chloro-.alpha.-phenylbenzyl)-, ethyl ester, dihydrochloride (6CI) (CA INDEX NAME)

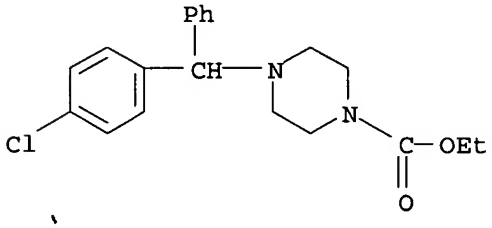


● 2 HCl

L9 ANSWER 7 OF 7 CAOLD COPYRIGHT 2003 ACS
AN CA51:5847a CAOLD
TI N-diarylmethylpiperazines
PA Abbott Laboratories
DT Patent

PATENT NO.	KIND	DATE
GB 752332		

IT **80476-89-7**
RN 80476-89-7 CAOLD
CN 1-Piperazinecarboxylic acid, 4-[(4-chlorophenyl)phenylmethyl]-, ethyl ester (9CI) (CA INDEX NAME)



```
=> log h
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    18.74     234.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -7.16

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:12:13 ON 16 JUL 2003
```